January 16, 2019

An Open Letter in Support of FDA's Clinical Study Report Pilot Project

In January 2018 the US Food and Drug Administration (FDA) launched a pilot project designed to enhance transparency around drug approval and assess the value of publicly disclosing Clinical Study Reports (CSRs). CSRs contain company-generated summaries of clinical trial methods and results, including more detailed information than the published literature. In March, one CSR underpinning the approval of a new drug was made available by the FDA with the consent of the sponsor, and posted on the FDA's website. At the time of the pilot's launch, up to eight additional CSRs were expected to follow.

The pilot project is an important step forward by the FDA. It marked a renewal of the FDA's longstanding authority to disclose regulatory data that is generally not publicly available. CSRs are, in fact, unabridged reports of clinical studies of pharmaceutical interventions. The reports exist for all clinical studies sponsors undertake (irrespective of whether such studies are eventually published in the biomedical literature) and are submitted to regulators as part of the licensing application. While FDA is furnished with additional data (such as electronic, participant-level datasets) and does not rely solely on CSRs to arrive at its decisions, disclosure of CSRs can help better explain the basis for FDA's decisions, and in turn, inform prescribers and patients about the evidence underlying a given drug.

Further, CSRs have enormous potential to improve public health by identifying unpublished, underreported, and misreported trials in the published medical literature. Consider the case of paroxetine (Paxil). On the strength of a 2001 article reporting the results of "study 329," paroxetine was widely prescribed for treatment of depression, including amongst teenagers. In 2002, however, an FDA reviewer (with access to the study 329 CSR) reported that the trial had shown the drug was not more effective than placebo—a report that was buried, even though publicly available, on the FDA's website. It was not until 2015, when independent researchers finally gained access to the full CSR, that the 2001 journal article results were effectively called into question through the republication of the trial. This is one of several cases in which the disclosure of CSRs can amplify important findings made by the FDA to the benefit of public health.

Despite the value of disclosing CSRs, a year after its launch the pilot project appears to have stalled. No additional CSRs have been posted on FDA's website.

We, the undersigned, therefore write to express our support for FDA's CSR Pilot Project. We urge the FDA to not only see the Pilot Project through to completion, but to make public disclosure of CSRs mandatory. The fact that only one company has volunteered to participate in the Pilot Project to date indicates that a policy of mandatory disclosure—a

policy that is already in place in Europe and is being implemented in Canada—is necessary to improve transparency of CSRs submitted to the FDA.

If FDA were to publicly disclose all CSRs following a decision to approve a new drug or biologic or a new indication for an existing drug or biologic, we will—as members of a research community dedicated to evidence-based medicine—use CSRs in the following ways for the purpose of improving public health: (1) to learn more about safety and efficacy evidence supporting FDA's approval decisions; (2) to include additional data from CSRs in systematic reviews along with other regulatory data; (3) to conduct methodological research to better characterize how to use CSRs in evidence synthesis; (4) to ensure the reports of trials in the biomedical literature (the building blocks for the majority of systematic reviews and clinical practice guidelines) are reported fully and accurately, with mechanisms available for public access to underlying data.

Matthew Herder, JSM LLM
Director, Health Law Institute
Dalhousie University

Peter Doshi, PhD
Assistant professor, Department of Pharmaceutical Health Services Research
University of Maryland School of Pharmacy

Joshua D. Wallach, MS, PhD
Assistant Professor, Department of Environmental Health Sciences
Yale School of Public Health

Janice E. Graham, PhD
University Research Professor
Dalhousie University

Joel Lexchin, MSc, MD
Professor Emeritus, Faculty of Health
York University

Trudo Lemmens, DCL
Professor, Faculty of Law
University of Toronto

Joseph S. Ross, MD MHS
Associate Professor of Medicine and Public Health
Yale University

Gregg Gonsalves, PhD
Assistant Professor, Yale School of Public Health
Yale University

Nav Persaud, MD, MSc
Assistant Professor, Department of Family and Community Medicine
University of Toronto

Peter Lurie, MD, MPH
President
Center for Science in the Public Interest

Huseyin Naci, MHS PhD
Assistant Professor of Health Policy
London School of Economics and Political Science

Mark Jones, PhD
Associate Professor, Faculty of Health Sciences & Medicine
Bond University

Tom Jefferson, MD
Senior Associate Tutor
University of Oxford

G. Caleb Alexander, MD, MS
Professor of Epidemiology and Medicine
Johns Hopkins Bloomberg School of Public Health

Erick H. Turner, MD
Associate Professor, Oregon Health & Science Univ
Dept of Psychiatry; Dept of Pharmacology
Senior Scholar, Center for Ethics in Health Care, OHSU

Evan Mayo-Wilson, DPhil, MPA
Associate Scientist, Center for Clinical Trials and Evidence Synthesis
Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health

Jennifer E. Miller, PhD
Assistant Professor, Yale School of Medicine
Founder, Bioethics International

PD Dr. med. Lars G. Hemkens MPH
Senior Scientist
Department of Clinical Research, University of Basel
University Hospital Basel

David Healy, MD
Professor of Psychiatry
Bangor University Wales

Jon Jureidini, MB BS, PhD
Professor, Disciplines of Paediatrics and psychiatry
University of Adelaide

Tianjing Li, PhD
Associate Professor, Department of Epidemiology
Bloomberg School of Public Health, Johns Hopkins University

Kay Dickersin, PhD
Professor Emeritus, Department of Epidemiology
Bloomberg School of Public Health, Johns Hopkins University

Aaron S. Kesselheim, M.D., J.D., M.P.H.
Associate Professor of Medicine
Brigham and Women's Hospital/Harvard Medical School